

A massive intraventricular thrombosis by disseminated mucormycosis in a patient with myelodysplastic syndrome during deferoxamine therapy

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A 70-year-old man with a 2-year history of myelodysplastic syndrome (MDS), refractory anemia, was hospitalized because of pneumonia. He had received frequent transfusions because of anemia. The total amount of blood transfusions he had received during the 7 months before admission was 44 units. In the previous 6 months, he had intravenously received 500 mg of deferoxamine after every transfusion to prevent secondary hemochromatosis (total dose: 6,500 mg). On admission, a complete blood count showed a white blood cell count of $2.0 \times 10^9 / L$ with 53% neutrophils, a hemoglobin level of 5.2 g/dL, and platelet count of $6 \times 10^7 / L$. The serum ferritin was 1,532 ng/ml indicating an iron overload state. Although he received a series of antibiotics and fluconazole as empiric therapy, his pneumonia progressed and pleural effusion became evident. Frequent microbiological investigations, including cultures of blood, sputum, and pleural fluids, and serum levels of endotoxin and β -D-glucan all yielded negative results. However, an intraventricular tumor mass was observed on echocardiogram on day 17 after admission, which had been undetectable 10 days before (Figure 1). Amphotericin B was started because of the suspicion of mucormycosis. However, he soon developed coma because of multiple cerebral infarctions on day 19, and died of cerebral hemorrhage on day 21. Autopsy revealed a large intraventricular thrombosis (Figure 2). Histopathologic findings of the thrombosis showed broad, irregularly-shaped, non-septal hyphae with right-angled branching, which is characteristic of mucormycosis (Figure 3). Disseminated mucormycosis was also detected in abscesses in multiple organs, including the brain, lung, liver, spleen, thyroid gland, and kidney. Mucormycosis is an opportunistic infection caused by *Mucorales zygomycetes*, mostly due to the inhalation of spores. Treatment with the iron chelator deferoxamine has been reported to be one of the risk factors for developing mucormycosis in patients with iron overload.^{1,2} In human plasma or on the mucosal surfaces, the amount of free iron available for microbial growth is

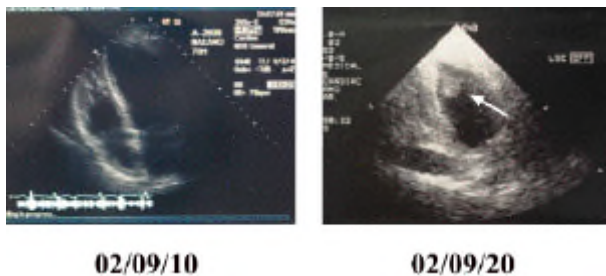


Figure 1. Echocardiography showed a large mass (arrow) in the left ventricle, although it had been undetectable just 10 days before.

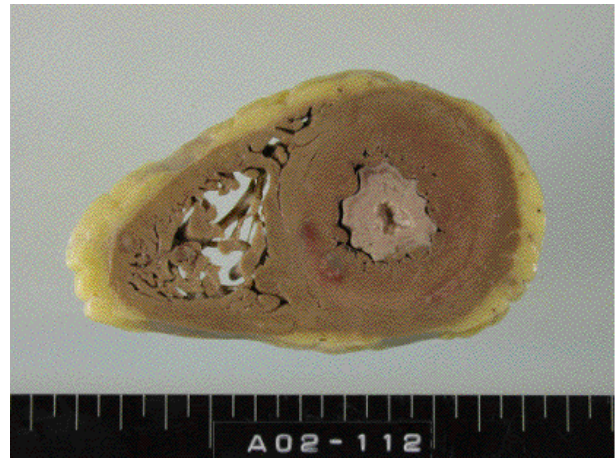


Figure 2. Macroscopic pathology of the heart shows a giant thrombosis in the left ventricle

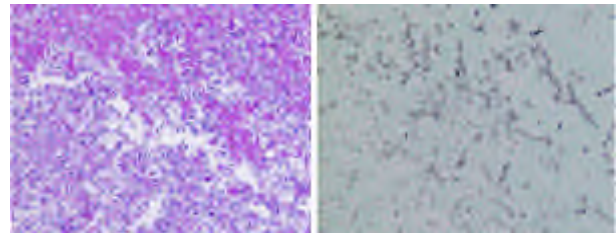


Figure 3. Histological examination of the left ventricular thrombosis demonstrates broad irregular hyphae, which are characteristic of mucormycosis. (left panel: PAS stain, right panel: Grocott stain, original magnification was X400)

low; almost all of the iron is bound to iron-binding proteins such as transferrin and lactoferrin or is inaccessible in tissue stores. Micro-organisms compete for the iron in the host, usually by secreting siderophores that trap iron and deliver it to the micro-organism, thus enhancing their growth. Deferoxamine B mesylate (deferoxamine) is one of the siderophores produced by *Streptomyces pilosus*. Therefore, administration of deferoxamine is suggested to extract iron to support the growth of the micro-organism for mucormycosis and thus result in infection.³ Mucormycosis was also reported in patients with hematologic malignancies such as leukemia, lymphoma, and bone marrow transplant recipients, without these patients having received deferoxamine therapy. However, these cases were reported to predominantly occur in the aplastic post-chemotherapy period.⁴ There are also some reports of mucormycosis in MDS patients not receiving deferoxamine.⁵ Therefore, we do not exactly know how much deferoxamine predisposed to mucormycosis in our case. However, caution should be taken to prevent mucormycosis in an immunocompromised host, especially those who are receiving deferoxamine for iron overload.

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